University of North Carolina-Chapel Hill
Consent to Participate in a Research Study
Adult Subjects

Medical IRB Study # 03-1139

Consent Form Version Date: April 25, 2007

Title of Study: Inflammatory Changes in Asthmatics Exposed to Concentrated Chapel Hill Coarse Air Particles

Principal Investigators: Neil Alexis, PhD., MHSc.
UNC-CH Department: Pediatrics
Phone number: 966-9915

Co-Investigators: David Peden, MD
Wayne Cascio, MD
Tony Huang, MD
Eugene Sanders, MD
Howard Kehrl, MD
Jim Samet, PhD
Robert Devlin, PhD
Andrew Ghio, MD

Study personnel: Martha Almond RRT, Margaret Herbst RN MSN; Carole Robinette MS, Hazel Shepherd RN MSN; Lynne Newlin-Clapp BA; Sally Ivins BA; CE Davis PhD, Maryann Bassett RN, Debbie Levin RN; and Tracey Montilla RN.

Sponsor: United States Environmental Protection Agency

You are being asked to take part in a research study. The investigators listed above are in charge of the study; other professional persons may help them or act for them.

What are some general things you should know about research studies?

Research studies are designed to gain scientific knowledge that may help other people in the future. You may or may not receive any direct benefit from participating. There may also be risks associated with participating in research studies.

Your participation is voluntary. You may refuse to participate, or may withdraw your consent to participate in any study at any time, and for any reason, without jeopardizing your future care at this institution or your relationship with your doctor. If you are a patient with an illness, you do not have to participate in research in order to receive treatment.

Details about this particular study are discussed below. It is important that you understand this information so that you can decide in a free and informed manner whether you want to participate. You will be given a copy of this consent form. You are urged to ask the investigators named above, or staff members who may assist them, any questions you have about this study at any time.

Initials _____

What is the purpose of this study?

The purpose of this research study is to determine if asthmatics exposed to coarse particles normally present in the outdoor air develop temporary inflammatory changes in their lungs or changes in their heart. Recent evidence in animals and humans have shown an association between inhaled particulate matter and altered cardiac function. These changes in cardiac function have been observed only in the elderly who may have pre-existing cardiopulmonary disease, as well as in persons exposed to higher than average levels of particulate air pollution in their workplace. Consequently, it is not expected that cardiac changes will occur in young otherwise healthy asthmatic persons. The levels of pollutants to which you will be exposed will not be higher than what you could be exposed to if you visited many major cities around the world.

How many subjects will participate in this study?

If you decide to participate, you will be one of up to 25, 18-40 year old asthmatic adults in enrolled in this study.

How long will your participation last?

Your participation in this study will last for approximately 5 weeks. You will undergo a screening process, including a medical examination, to make sure you are eligible for the study and don't have any underlying medical problems that could place you at undue risk for participating in the study. To participate in the study, you will need to visit our facility on 5 occasions. During your **first visit**, which will last about an hour, we will describe the study to you in detail and you will be given an opportunity to ask any questions you may have about the study. We will also familiarize you with the exposure chamber and how to perform things like ride an exercise bike or have your lung function measured by blowing in a tube. On your **second visit**, you will be here about **5 hours** during which you will be exposed to clean air or Chapel Hill air pollution particles. You will return the next day **(third visit)** for an additional 4 hours, during which you will undergo bronchoscopy. Then after about a month has passed you will return for your **fourth and fifth visits** in that on the first day you will be exposed to either air or particles and the next day you will undergo bronchoscopy. During each of these last four visits you will have a small amount of blood drawn, and electrodes placed on your chest to monitor your heart.

For the exposure days you will be exposed once to clean air and once to air containing air pollution particles present in Chapel Hill air. Each of the exposure periods will be for two hours, during which you will exercise on a stationary exercise bike in the exposure chamber. You will also have some blood drawn before and after each exposure and electrodes placed on your chest to monitor your heart. The total time you will be present in our facility on each of those days will about 4 hours. You will also need to return the morning after each exposure for follow-up tests on your blood and heart and to undergo bronchoalveolar lavage; this will also take about 4 hours. The two exposure sessions will be separated by at least 4 weeks.

Initials _____

What will happen if you take part in the study?

During the course of this study, the following will occur:

You will be given a physical examination to determine if you are eligible to participate in this study. This study requires that you have no significant problems with your nose, throat, heart, lungs, or blood.

You will be reminded by telephone a few days before the exposure session. The day before exposure until the day following exposure you are asked to refrain from alcohol, excessive amounts of caffeine, and from any activities where you could be exposed to high levels of pollutants (e.g. cigarette smoke, paint fumes). Please report any pollutant exposure to the study personnel so you can be rescheduled if necessary.

On the day of exposure, you will report to the medical station in the Human Studies Facility where the nurses will take your temperature and ask questions about any symptoms or recent acute illnesses. You will be rescheduled if you have experienced an upper or lower respiratory tract illness within the past 6 weeks, or any other acute illness within the past week. Women will be asked about their latest menstruation and a urine pregnancy test will be conducted. If you are pregnant your participation will be terminated and you will receive full compensation for the exposure day. Venipuncture (blood draw) will be performed by routine medical procedure. A nurse will draw blood from your arm before and after your exposure to air or particles. A small portion of the blood (2.7 ml) taken at the pre-exposure time will be used to look for genes (GSTM1) and specific products of those genes that are involved in inflammation and anti-oxidant defense mechanisms. We'll be looking to see whether the GSTM1 gene is present or absent in a particular genomic DNA sample. Samples used for genetic analysis will be stored at the EPA Human Studies Facility (HSF) or the Center for Environmental Medicine, Asthma and Lung Biology at UNC-Chapel Hill (CEMALB) located within the HSF. A numeric coding system will be used to ensure that you cannot be directly identified from the samples alone. You will be asked to sign an additional consent form for ***Storing Biological Specimens With Identifying Information*** which will provide you with additional information regarding samples we collect from you during this study. During the course of this research, other researchers may request access to specimens (or data) for as-of-yet unspecified research that may or may not be related to the original research from which the specimens were derived. In these cases, provided appropriate UNC IRB approved consent has been obtained from subjects, these specimens (or data) will be provided without identifiers to these other researchers by employing a Data Use Agreement or Honest Broker model.

The nurses will also attach electrocardiograph (ECG) leads to your chest. It may be necessary to clean and shave the areas of you chest where these leads will be placed. The leads will be connected to 2 monitors (small recording devices about the size and weight of a portable tape player) to obtain readings of your heart rate and function. One of these monitors will be removed when you leave for the day. The other monitor, a Holter monitor, will remain connected to you until you return the next day. An oximeter (small band like device that fits on your fingertip) will also be used to allow the medical staff to monitor your oxygen levels while you are in the chamber. You will not be able to shower or bathe until after the Holter monitor is removed when you return the next morning. You will be asked to recline quietly for 30 minutes and to breathe

Initials _____

at a constant rate while a measurement of your heart rate is taken by the Holter. It is important that you do not fall asleep during this 30-minute period. Next, a small blood sample (about ¼ cup) will be taken from your arm and you will also be asked to blow into a tube to check the function of your lungs.

You will then enter the exposure chamber (4 x 4 x 6 feet in size) and be exposed to either clean air or air containing air pollution particles. The amount of particles you will be exposed to will depend on the amount of pollution in the air in Chapel Hill on the day of your exposure. While in the exposure chamber you will be asked to exercise on a bicycle ergometer 15 minutes, followed by 15 minutes of rest. This pattern will be repeated during the two hour period of time you are in the chamber. You will be directed to pedal at a speed fast enough to cause an approximate doubling of your normal resting heart rate. A physician or a trained investigator will be seated outside the chamber to observe you at all times. A physician will be on call in the facility during the entire exposure session. During the exposure, your heart will be monitored. If it appears you are experiencing significant breathing or heart problems, or you develop any symptoms of discomfort (e.g. severe headache, nausea, vomiting, fever) the exposure will be terminated immediately. In addition, you may elect to terminate the exposure at any time for any reason. If you do so, you will be paid in full for that day's session, but will be ineligible for further participation in the study and any payments you would have received for future participation. We may also elect to terminate a study for any reason; however, if we do so, you will be paid in full for your participation up to that point.

Immediately after the exposure you will again blow into a tube to determine if the exposure caused changes in your lung function. Then you will again recline quietly for 30 minutes while your heart rate is measured and another blood sample will be taken. You will be asked to wear the Holter monitor with the electrodes attached to your chest until you return the next morning. It will take continuous readings from your heart during the entire time it is attached. In addition, it is very important that you take nothing by mouth (including water) after midnight. For your own safety, you will not be allowed to participate in the bronchoscopy if you do.

The next morning you will return to the EPA facility for additional heart rate analysis, blood-work, and the bronchoscopy. The nurses will check you in and the study physician who is board certified in pulmonary medicine will ask if you encountered any difficulties. You will be allowed to rest quietly for 30 minutes for heart rate analysis after which a blood draw will take place and the Holter monitor will be removed. Separate leads will be placed so that your heart rate and function can be monitored during the bronchoscopy procedure. Before undergoing bronchoscopy, you may at the study physician's discretion, be treated with an inhaled bronchodilator and your lung function will be evaluated. The procedure will not be performed if the study physician determines your lung function does not exceed a predetermined level of function recommended by the National Institute of Health for performing research bronchscopies in persons with asthma. Intravenous atropine (0.6mg) may, at the study physician's discretion, be given in a vein in your arm before the procedure starts. The nurses will then lightly anesthetize your nasal passages and throat. A bronchoscope (similar to a thin plastic tube) will be inserted by study physician through your nose and passed through the back of your throat to reach the trachea (windpipe) and the airways leading to the lungs. To reduce coughing and discomfort you

Initials _____

will gargle and inhale an anesthetic (topical lidocaine) prior to beginning the procedure. During the procedure you will also receive supplemental oxygen. If any adverse reactions occur, prompt corrective action will be initiated. After the bronchoscope is inserted sterile saline will be used to wash out a small portion of your lung (about 1/64 of your lung). At the discretion of the investigator, a tiny brush with flexible bristles will be rubbed against the side of your airways a few times to remove some cells. The materials obtained during bronchoscopy will be used to determine if air pollution particles affected the cells and fluids in your lung. You should not feel any pain during these procedures, though you may feel the urge to cough. Following the bronchoscopy, you will need to remain for a suitable observation period. When a physician has determined that you are fully recovered, which may include having spirometry (lung function) rechecked and compared to your pre-procedure value, you will be discharged. During this observation period you will be offered snacks and drinks.

Are there any reasons you should not participate?

You should not participate in this study if you are unhealthy or pregnant. You need to be non-smoker for at least 1 year prior to the study and have not smoked or smoked only a little earlier in your life. There are several medical conditions that may prevent you from participating in this study. These include, but are not limited to, active allergies, diabetes, need for a pacemaker, a previous heart attack or coronary bypass surgery, dialysis treatment, or the need for supplemental oxygen. In addition, if you take certain medications, (either prescription or over-the-counter) that may affect our ability to interpret your response to particles you will be asked to stop taking them for one week prior to your exposure sessions. These may include things such as anti-inflammatory drugs such as aspirin or anti-oxidants. If you are unable to stop taking your medications, you will not be eligible for the study

What are the possible risks or discomforts?

This study might involve the following risks and/or discomforts to you:

There are several risks associated with performing bronchoscopy, although these risks are exceedingly small when bronchoscopy is performed on young healthy subjects by a qualified physician. The primary risk of bronchoscopy is coughing and discomfort in the nose and throat, which is caused by having the bronchoscope inserted through the nose and passed through your throat. This discomfort and coughing is alleviated with topical lidocaine, which you will gargle and inhale prior to beginning the procedure. If you are unable to tolerate the passage of the bronchoscope through your nose and throat because of pain or uncontrollable coughing in spite of having received the maximum allowable amount of lidocaine, the procedure will be immediately terminated.

The lidocaine used for anesthesia during the procedure may result in some adverse effects due to absorption into the blood stream from the nose and the lungs. Lidocaine can cause symptoms in your central nervous system (confusion, tremor, euphoria, or, rarely, seizure) or heart rate disturbances (very fast or very slow heart rate) if an excessive dose of medication is used. The topical doses of lidocaine in this study will be low (no higher than 300 milligrams) so we do not expect significant systemic absorption to occur. If you are allergic to lidocaine, you could develop itching, hives, difficulty breathing, and possibly shock (a drop in blood pressure). This risk is minimal, but you will be excluded from the study if you are allergic to lidocaine or any

Initials _____

other topical anesthetic that is commonly used in minor surgical or dental procedures. You should know that a volunteer receiving a large lidocaine overdose (over 1000 milligrams) during bronchoscopy in Rochester, New York died as a result of the overdose. However, no serious side effects of this medication have been noted at lower doses such as those described in this protocol and one of the nurses who assist during the bronchoscopy carefully monitors the amount of lidocaine to which you are exposed (241mg – 297milligrams).

On very rare occasions, bronchoscopy can cause an asthmatic attack, characterized by wheezing, chest tightness, and shortness of breath. This type of complication is very, very rare in subjects who have no history of asthma or other lung diseases. If an asthma attack occurs, the bronchoscope will be removed, and inhaled medication used to treat asthma (e.g. albuterol) will be given. These steps are usually all that is necessary to terminate the attack. However, if further care is needed, you will be transferred by ambulance to the Emergency Room at University of North Carolina Hospital.

Bleeding from the nose can also occur as a result from bronchoscopy. It is usually caused by injury from the bronchoscope within the nostril. This type of bleeding is almost always very minor, causing streaking of the nasal mucus, which resolves spontaneously within an hour or so after completion of the bronchoscopy. On extremely rare occasions, moderate to severe nose bleeding would require packing your nose with sterile gauze and transferring you to the Emergency Room at University of North Carolina Hospitals. Aspirin products (including BC Powders or Goodys Powders) and anti-inflammatory medications such as Motrin (ibuprofen) and Naprosyn (naproxen) may cause an increased tendency to bleeding. It is essential that you not take these types of medications for at least one week prior to bronchoscopy (acetaminophen [Tylenol] is acceptable).

Another risk that can occur from performing bronchoscopy is pneumothorax (collapsed lung). This may occur when biopsies (tissue samples) are being taken. In the very unlikely event that a pneumothorax does occur, you must be aware of the symptoms that it can cause: chest pain and shortness of breath. If these symptoms do occur after your bronchoscopy, you must contact the EPA physician who performed the bronchoscopy immediately. His name and telephone number are on the discharge sheet you will be given when you leave the facility. If pneumothorax occurs after bronchoscopy, it usually occurs within 24 to 48 hours after the procedure is completed.

Some subjects who undergo bronchoscopy may have a low-grade fever (less than 101 degrees Fahrenheit) after the procedure is completed. This fever is almost always benign, and it occurs in approximately 25 percent of all subjects who undergo bronchoscopy. This fever usually resolves within 24 hours with the use of Tylenol. Nevertheless, a persistent fever or any temperature of greater than 101 degrees Fahrenheit might mean that you have an infection. Therefore, if you have any fever greater than 101 degrees Fahrenheit after the bronchoscopy or a fever that doesn't resolve within 24 hours after the procedure is completed, you should contact the physician who performed the bronchoscopy so that arrangements can be made for you to be examined.

Finally, there is a small possibility (less than 1 percent) that you might get pneumonia as a result of bronchoscopy in which bronchoalveolar lavage is performed. The signs and symptoms

Initials _____

of pneumonia include: 1) fever greater than 101 degrees Fahrenheit or persistent fever, 2) persistent cough with or without sputum production, 3) chest pain, 4) shortness of breath with exercise or at rest, 5) coughing up of blood. If you experience any of these symptoms after bronchoscopy, you should contact the EPA medical station or the physician who performed the bronchoscopy so that arrangements can be made for an examination by an EPA physician. You will be contacted 24 to 48 hours after the bronchoscopy to see if you are experiencing any of the above mentioned problems or any new health problems that you think could be related to bronchoscopy. In addition, there may be uncommon or previously unrecognized risks that might occur.

If you have any tendency to become uncomfortable in small closed spaces, it is possible that you may become uncomfortable during this study. You will be taken to the exposure chamber when you are first evaluated for suitability for the study to allow you an opportunity to see where you will sit and what the chamber looks like.

During one of your exposure sessions you will be exposed to air pollution particles. Some studies suggest that elderly people, particularly those with underlying cardiovascular disease, may be at increased risk for developing illness or even dying as a result of exposure to particles. However, the risk is much less for young healthy people. At this time, no one understands exactly how particles might cause increased risk of disease or death, but the risk to any one person, especially a young healthy person, are extremely small. While we cannot exclude the possibility that you may have an adverse reaction to breathing these particles, you will only be exposed to them for a 2 hour period and they will not exceed levels you might encounter if you were to visit many major cities around the world on a smoggy day.

There are very minimal risks associated with the lung function measurements in which you blow through a tube. One of the lung function tests requires that you inhale a gas mixture containing 0.3% carbon monoxide, 0.3% methane, and 0.3% acetylene. Although inhalation of carbon monoxide can be dangerous to your health at high concentrations (>10%) over several minutes, the concentrations used in these tests (0.3%) is not dangerous and is very unlikely to cause symptoms that are typically associated with carbon monoxide poisoning (i.e. headache, nausea, and dizziness). Methane is an inert gas and has small effects at high concentrations. Acetylene is a gas that at high concentrations may cause headache and dizziness. However, the concentrations of the gas mixture you will inhale are quite low and you will inhale them only for a very short time. The inhalation will be stopped immediately should you develop any of the following symptoms: headache, nausea, dizziness or general discomfort.

There are very minimal risks associated with monitoring your heart by ECG or blood oxygen by pulse oximetry. Preparing your skin for placement of ECG electrodes and removing the electrodes the next day may cause some irritation, itching, or burning in some people. If this occurs call the nursing staff.

The risks associated with taking blood samples are considered minimal.

Initials _____

Loss of confidentiality about genetic information is a study risk, but mechanisms in place to maintain confidentiality as well as the fact that the genetic information obtained in this study is not for disease diagnostic purposes, should make incurring this risk and its impact minimal.

What are the possible benefits?

The benefits to you of participating in this study include a medical examination that includes blood work, lung function testing, and baseline ECG at no charge. However, this is not a substitute for a routine doctor visit. A member of the medical staff will explain to you any remarkable findings regarding your overall health status. In addition, if we observe changes in your heart rate or lungs as a consequence of exposure to air pollutants, you may elect to use this information to avoid exposure on high pollution days. The primary benefit to society produced by this study will be a better understanding of whether or how air pollution particles affect people with asthma. Given that at least 5% of Americans suffer from asthma and are exposed to these pollutants, this study has the potential to contribute to devising effective strategies aimed at protecting millions of asthmatics from the untoward effects of these particles.

What if we learn about new risks during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will your privacy be protected?

No subjects will be identified **by name** in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-CH will take all steps allowable by law to protect the privacy of personal information.

Will you be paid for participating?

You will be paid $15.00 for time spent in your initial interview to determine if you are interested and qualify to participate in the study. In addition you will be paid $15.00 for your physical examination and $20.00 for your bronchoscopy exam. If you qualify for the remainder of the study, you will receive payment for your participation at the rate of $12.00 per hour (with the exception of time spent inside the exposure chamber which is $36.00/hr). You will need to be at the Human Studies Facility approximately 5 hours for each exposure session, including 2 hours in the exposure chamber itself. You will also need to return to the EPA facility the next morning for follow-up procedures which will take about four hours. You will also be paid $25 every time we draw blood during the study and $100 every time you wear the Holter monitor overnight. You will be paid $325 for each bronchoscopy, which will include washing a small portion of your lung with sterile saline, and if a brush biopsy is performed (at the investigator's discretion) to obtain a small number of cells with a cytology brush, you will paid an extra $25.00. You are also entitled to a $50 bonus if you complete the entire study. The total compensation if you complete this study should be approximately $1474. In addition, you will be reimbursed for reasonable travel expenses and for parking costs at the UNC campus.

Initials _____

The following table details the expected compensation for completion of the entire study:

Initial Screening for Eligibility	$15
Physical Exam	$15
Bronchoscopy Physical Exam	$20
Training	$12
Exposure Sessions (2 for 5 hours each) (Check-in, pre-testing, exposure, post-testing)	$216
Next day Follow-up (2 x 4 hours)	$96
Blood samples (6)	$150
24-hour ambulatory ECG monitor (2)	$200
Bronchoscopy (2) (BAL, cytology brushes, biopsy, recovery)	$700
Bonus for Completing the Study	$50
Total Compensation	$1474

It is possible that on some days (e.g. when it is raining) there may not be enough air pollution particles in the air to allow the study to proceed. If that happens during one of your visits, you will be rescheduled and receive compensation ($12/hr) for the time scheduled and canceled, and will be paid 50% up to a maximum of $100 for canceled procedures. Cancellations could occur due to adverse weather conditions, equipment failure, or other unforeseen events. When feasible the subject will be rescheduled. In addition, you will be reimbursed for reasonable travel expenses and for parking costs at UNC.

You understand that your participation is voluntary. You may terminate your participation in the study at any time without penalty, and without losing benefits you would otherwise be entitled to. If you elect to terminate your participation in the study, you will be paid for that portion of the study, which has been completed. The investigators also have the right to stop your participation in the study at any time. This could be because you have had an unexpected reaction, or because the entire study has been stopped or for some other reason. If this occurs, you will be paid for your participation up to that point.

Will it cost you anything to participate?

The U.S. EPA will pay the costs of this research. You will not be billed for any procedures. However, if you are deemed not eligible to participate in the study for medical reasons, we may recommend that you seek follow-up care from your own health care provider for abnormalities discovered during the screening history and physical examination. Such care is entirely at your own expense. EPA will not provide reimbursement for any follow up care.

What will happen if you are injured by this research?

All types of research involve possible risk, some including the risk of personal injury. In spite of all precautions, you might develop complications from participating in this study. If such complications arise, the researchers will assist you in obtaining appropriate medical treatment, but any costs associated with the treatment will be billed to you and/or your insurance company. Neither the University of North Carolina at Chapel Hill nor the U.S. EPA has set aside funds to pay you for any such reactions or injuries, or for the related medical care. If you believe you have suffered a research-related injury, you have the right to pursue legal remedy if you believe

Initials _____

that your injury justifies such action. The Federal Tort Claims Act, 28 U.S.C. S 2671 et seq., provides for money damages against the United States when property loss or personal injury results from the negligent or wrongful act or omission of any employee of the EPA while acting within the scope of his or her employment. Signing this consent form does not waive any of your legal rights or release the investigator, the sponsor, the institution, or its agents from liability for negligence. If a research-related injury occurs, you should contact the Director of the EPA NHEERL Human Research Protocol Office at 919-966-6217.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have further questions, or if a research-related injury occurs, you should call one of the listed investigators: Neil Alexis, PhD.919-966-9915; David Peden, MD. 919-966-0768; Robert Devlin, Ph.D. 919-966-6255; Tony Huang, M.D. 919-843-9504

What if you have questions about your rights as a subject?

This research has been reviewed and approved by the Committee on the Protection of the Rights of Human Subjects (Medical IRB) at the University of North Carolina at Chapel Hill. If you have any questions or concerns regarding your rights as a research subject, you may contact the Chairman of the IRB Committee at 919- 966-1344 and/or the Director of the EPA NHEERL Human Research Protocol Office at 919-966-6217.

- -

Subject's Agreement:

I have read the information provided above. I voluntarily agree to participate in this study.

__________________________________ ________________
Signature of Research Subject Date

____
Printed Name of Research Subject

__________________________________ ________________
Signature of Person Obtaining Consent Date

____
Printed Name of Person Obtaining Consent

University of North Carolina at Chapel Hill
Consent for Storing Biological Specimens With Identifying Information

---

IRB Study # 03-1139
Consent Form Version Date: April 25, 2007

Title of Study: Inflammatory Changes in Asthmatics Exposed to Concentrated Chapel Hill Coarse Air Particles

Principal Investigators: Neil Alexis, PhD., MHSc.

UNC-Chapel Hill Department: Center for Environmental Medicine, Asthma and Lung Biology and Pediatrics

UNC-Chapel Hill Phone number: 966-9915

Co-Investigators: David Peden, MD
Wayne Cascio, MD
Tony Huang, MD
Eugene Sanders, MD
Howard Kehrl, MD
Jim Samet, PhD
Robert Devlin, PhD
Andrew Ghio, MD

Funding Source: United States Environmental Protection Agency.

Study Contact telephone number: 966-2879
Study Contact email: margaret_herbst@med.unc.edu

What are some general things you should know about this research study?
Research studies are designed to gain scientific information that may help other people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Research with blood, tissue and/or body fluids (specimens) can help researchers understand how the human body works. Research using specimens can also answer other questions. Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat diseases. In the future, some research may help to develop new products, such as drugs.

You may refuse to allow us to have or store your specimen. If you are a patient with an illness, you do not have to be in the research study in order to receive treatment.

Details are discussed below. It is important that you understand this information so that you can make an informed choice. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?
The purpose of this study is to store coded excess samples collected as part of the main study for future research. Researchers in the future may want access to these samples to study questions related to human health and the effect of various agents on humans as well as for future currently undesignated studies including possible genetic research. Samples to be stored may include specimens such as blood, tissue, body fluids, and sputum samples which remain after these samples have been collected and analyzed as part of the main

How will the specimen be collected?
The description of the samples to be collected and the manner in which this will be done have been described in the main study consent.

What will happen to the specimen?
If there are excess samples left over after use for the purposes of this specific study, they will be stored in a refrigerator, freezer or as slides in the Environmental Protection Agency (EPA) Human Studies building.

During the course of this research, other researchers may request access to specimens (or data) for as-of-yet unspecified research that may or may not be related to the original research from which the specimens were derived. In these cases, provided appropriate UNC IRB approved consent has been obtained from subjects, these specimens (or data) will be provided without identifiers to these other researchers by employing a data use agreement or Honest Broker model.

What are the possible benefits to you?
Benefits to you are unlikely. These studies (current and future) may provide additional information that will be helpful in understanding questions related to human health and the effect of various agents on humans with asthma.

What are the possible risks or discomforts involved with being in this study?
Risks associated with venipuncture and sputum collection have been outlined in the main study consent. The risks associated with a breach of confidentiality are minimized by the protections discussed below.

Will there be any cost to you for storage of the specimens?
There will be no cost to you for the storage and use of the specimens for research purposes.

Will you receive anything for being in this study?
You will not receive anything for taking part in this study with regard to storage of excess specimens. Reimbursement for participation in the main study is addressed in the detailed consent for that study.

Who owns the specimens?
Any blood, body fluids, or tissue specimens obtained for the purpose of this study become the exclusive property of EPA and the Center for Environmental Medicine, Asthma and Lung Biology. The researchers may retain, preserve or dispose of these specimens and may use these

specimens for research that may result in commercial applications. There are no plans to compensate you for any future commercial use of these specimens.

How will your privacy be protected?

Your identifiable data will be protected by use from future investigators by either and Honest Broker system or a data use agreement. In the case of the Honest broker system your identifiable data will be secured in the medical station, and future investigators who wish to use your coded samples will not have access to this data. The medical station staff will not, under any circumstances (except as required by law), provide this information to future researchers. Alternatively, coded samples or data may be used by future researches if a data use agreement is established between the investigator(s) for this study and the future researcher. In this agreement, the investigator associated with the current study agrees to withhold all personal identifying data from the future investigator and will release only samples or data which are coded.

As a part of this research study, the research team will review your medical records. The research team includes the researchers named on the first page of this form, and their assistants. You will sign a separate HIPAA authorization form for a review of your medical records information.

The coded specimens may be shared with other outside research groups, both within the EPA and University of North Carolina System or outside of these locations. Research studies may be done at many places at the same time. Your personal identifying information will not be sent to outside researchers.

No one will be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies for purposes such as quality control or safety.

Will researchers seek approval from you to do future studies involving the specimens?

By signing this consent form, you are giving your permission for researchers to use your specimens as described above. Current and future research is overseen by a committee called the Institutional Review Board (IRB). The role of the IRB is to protect the rights and welfare of research participants.

In some cases, the IRB may require that you be re-contacted and asked for your consent to use your specimens in a specific research study. You have the right, at that future time, not to participate in any research study for which your consent is sought. Refusal to participate will not affect your medical care or result in loss of benefits to which you are entitled.

Will you receive study results of future research involving your specimens?
Most research with your specimens is not expected to yield new information that would be meaningful to share with you individually. In rare cases, you may be offered the opportunity to receive information about the results of research in which the specimens were used (for example, findings that would affect your medical care).

Can you withdraw the specimens from the research study?
If you decide that you no longer wish for the specimens to be stored, you should contact the researchers on the front page of this form. You may also contact the Institutional Review Board, University of North Carolina at Chapel Hill, 919-966-3113, Medical School Building 52, CB 7097, Chapel Hill, NC 27599, or by email at IRB_subjects@unc.edu. It is best to make your request in writing.

Any analysis in progress at the time of your request or already performed prior to your request being received by the researcher will continue to be used as part of the research study. Once the researchers have been notified, your specimens would be destroyed. If you do not make such a request, the specimens may be stored forever. The researchers may choose to destroy the specimens at any time.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from having your specimen collected. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. However, by signing this form, you do not give up any of your legal rights. The Federal Tort Claims Act, 28 U.S.C. S 2671 et seq., provides for money damages against the United States when property loss or personal injury results from the negligent or wrongful act or omission of any employee of the EPA while acting within the scope of his or her employment. Signing this consent form does not waive any of your legal rights or release the investigator, the sponsor, the institution, or its agents from liability for negligence. If a research-related injury occurs, you should contact the Director of the EPA NHEERL Human Research Protocol Office at 919-966-6217.

.

Who is sponsoring this study?
This research is funded by research collaborations with National Center for Complementary and Alternative Medicine, as well as the US Environmental Protection Agency. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions, you should contact the researchers listed on the first page of this form or Dr. Richard Hermann (919-966-6217), EPA Director of the National Health and Environmental Effects Human Research Laboratory Protocol Office.

What if you have questions about your rights as a research subject?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject you may contact, anonymously, if you wish, the Institutional Review Board at 919-966-3113 or by email to IRB_ subjects@unc.edu and/or the Director of the EPA NHEERL Human Research Protocol Office at 919-966-6217.

Subject's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate. I agree to my specimen(s) being stored with the identifying code(s).

_____ _____

Signature of Research Subject Date

_____

Printed Name of Research Subject

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent